PTO/SB/05 (08-00)
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### UTILITY PATENT APPLICATION **TRANSMITTAL**

(Only for new nonprovisional applications under 37 CFR 1.53(b))

Attorney Dock	et No.	05871.0010.CNUS03				
First Inventor		Thomas M. Brennan				
Title		Method and Apparatus for Performing Large Numbers of Reactions				
Express Mail	:	EL615212541US				

APPLICATION ELE	MENTS	Commissioner for Patents  ADDRESS TO: Box Patent Application					
See MPEP Chapter 600	concerning utility patent application contents.	Washington, DC 20231					
(Submit an origination of the control of the contro	De Related Applications ling Fed Sponsored R & D lence listing, a table, ligram listing appendix Invention the Invention	7. □ CD-ROM or CD-R in duplicate, large table or Computer Program (Appendix)  8. ☑ Nucleotide and/or Amino Acid Sequence Submission (if applicable, all necessary)  a. □ Computer Readable Form (CRF)  b. Specification Sequence Listing on:  i. □ CD-ROM or CD-R (2 copies); or  ii. □ paper  c. ☑ Statements verifying identity of above copies  ACCOMPANYING APPLICATION PARTS					
Abstract of the Di	sclosure S.C. 113) [Total Sheets 30 ]						
5.  Oath or Declarating a.  Newly exect b.  Copy from a (for continual in DELET) Signed an angular signed in 1.63(d)(2).  17. If a CONTINUING AP Application Data Sheet un Continuation Information Prior application informatic	puted (original or copy) a prior application (37 CFR 1.63 (d)) ational divisional with Box 17 completed) ION OF INVENTOR(S) statement attached deleting inventor(s) in the prior application, see 37 CFR 2) and 1.33(b). Sheet. See 37 CFR 1.76  PLICATION, check appropriate box, and supply the required are 37 CFR 1.76:  Divisional Continuation-in-part (CIP) Divisional Framiner Jefffrey Siew Group DIVISIONAL APPS only: The entire disclosure of the	9. Assignment papers (cover sheet & document(s))  10. 37 CFR 3.73(b) Statement Power of (when there is an assignee) Attorney  11. English Translation Document (if applicable)  12. Information disclosure Copies of IDS Statement (IDS)/PTO-1449 Citations  13. Preliminary Amendment  14. Return Receipt Postcard (MPEP 503) (Should be specifically itemized)  15. Certified Copy of Priority Document(s) (if foreign priority is claimed)  16. Other:  isite information below and in a preliminary amendment, or in an of prior application No.: 09/686,597 filed October 10, 2000  1 Art Unit: 1637  prior application, from which an oath or declaration is supplied under					
Box 5b, is considered a p	part of the disclosure of the accompanying continuat any be relied upon when a portion has been inadverte	ion or divisional application and is hereby incorporated by reference.					
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Signature	Milita	Date June 23, 2003					

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TOTAL AMOUNT OF PAYMENT



1. PTO/SB/17 (09-00)
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## FEE TRANSMITTAL For FY 2002

Patent fees are subject to annual revision.

(\$) 551.00

Complete if Known				
Application Number	Not yet Assigned			
Filing Date	June 23, 2003			
First Named Inventor	Thomas M. Brennan			
Examiner Name	Jeffrey Siew			
Group Art Unit	1637			
Attorney Docket No.	05871.0010.CNUS03			

METHOD OF PAYMENT					FEE CALCULATION (continued)								
1.   The Commissioner is hereby authorized to charge indicated fees and credit any overnayments to:					3. ADDITIONAL FEES								
Deposit Acct. No. 08-3038				Large Fee	Entity Fee	Small Fee	Entity Fee	Fee Description	Fee Paid				
Deposit					105	130	205	65	Surcharge - late filing fee or oath				
Account Name Howrey Simon Arnold & White, LLP					127	50	227	25	Surcharge – late provisional filing fee or cover sheet				
Charge Any Additional Fee Required					139	130	139	130	Non-English specification				
Under 37 CFR 1.16 and 1.17					147	2,520	147	2,520	For filing a request for ex parte reexamination				
Applicant claims small entity status. See 37 CFR 1.27					112	920*	112	920*	Requesting publication of SIR prior to Examiner action				
2. 🗵 Payment Enclosed:					113	1,840*	113	1,840*	Requesting publication of SIR after Examiner action				
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Order					116	400	216	200	Extension for reply within second month				
FEE CALCULATION					117	920	217	460	Extension for reply within third month				
1. BASIC	FILIN Entity	IG FEE	Entity					118	1,440	218	720	Extension for reply within fourth month	
Fee	Fee	Fee	Fee	Fee	Description	1		128	1,960	228	980	Extension for reply within fifth month	
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106	330	201	165	_	_	F	375.00	120	320	220	160	Filing a brief in support of an appeal	
107	510	207	255	_	n filing fee iling fee	⊢		121	280	221	140	Request for oral hearing	
108	740	208	370		ing ree ie filing fee	⊢		138	1,510	138	1,510	Petition to institute a public use proceeding	
114	160	214	80		ional filing fe	⊢		140	110	240	55	Petition to revive – unavoidable	
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								142	1,280	242	640	Utility issue fee (or reissue)	
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2. EXTR	A CLA	IM FE						144	620	244	310	Plant issue fee	
			Extra Claims		Fee from below		Fee Paid	122	130	122	130	Petitions to the Commissioner	
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Independent	$\vdash$		<b>—</b>	╡		╡		126	180	126	180	Submission of Information Disclosure Stmt	
Claims Multiple Depe	1 ndept	- 3**=	0	×	42	┥		581	40	581	40	Recording each patent assignment per property (times number of properties)	
.nampie pepe					140		140	146	740	246	370	Filing a submission after final rejection (37 CFR § 1.129(a)	
Large Fee Code	Entity Fee	Small Fee Code	Entity Fee		Fee De	scriptic	on	149	740	249	370	For each additional invention to be examined (37 CFR § 1.129(b)	
103	(\$) 18	203	(\$) 9	Claims	in excess of 2	:0		179	740	279	370	Request for Continued Examination (RCE)	
102	84	202	42		Independent claims in excess of 3		169	900	169	900	Request for expedited examination		
104	280	204	140		Multiple dependent claim, if not paid							of a design application	
109	80	209	40	** Reissue Independent claims			Other fee (specify)						
over original patent			* Reduced by Basic Filing Fee Paid SUBTOTAL (3) (\$)0										
110 18 210 9 ** Reissue claims in excess of 20 and over original patent				]									
SUBTOTAL (2) (\$)176.00													
**or number previously paid, If greater; For Reissues, see above													

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SUBMITTED BY			Complete (if applicable)
Name (Print/Type)	Albert P. Haluin, Wallace Wu	Registration No. (Attorney/Agent) 25,227, 45,380	Telephone 650-463-8109
Signature	MIL MA	_	Date June 23, 2003

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# METHOD AND APPARATUS FOR PERFORMING LARGE NUMBERS OF REACTIONS USING ARRAY ASSEMBLY

This application claims priority to U.S. Provisional Application Serial

No. 60/158,315, filed October 8, 1999 and to U.S. Application Serial No. 09/686,597, filed October 10, 2000.

#### FIELD OF THE INVENTION

The present invention relates to a method and apparatus for performing a large number of reactions using array assembly. In particular, the present invention features a method and apparatus for performing a large number of chemical and biological reactions by bringing two arrays into close apposition and allowing reactants on the surfaces of two arrays to come into contact. The present invention is exemplified by performing a large number of polynucleotide amplification reactions using array assembly. In addition, the present invention features a method and apparatus for coupling the amplification of polynucleotides and the detection of sequence variations, expression levels, and functions thereof.

### **BACKGROUND OF THE INVENTION**

Intense efforts are under way to map and sequence the human genome and the genomes of many other species. In June 2000, the Human Genome Project and Celera Genomics announced that a rough draft of the human genome had been completed. This information, however, represents only a reference sequence of the 3-billion-base human genome. The remaining task lies in the determination of sequence variations (e.g., mutations, polymorphisms, haplotypes) and sequence functions, which are important for the study, diagnosis, and treatment of human genetic diseases.

In addition to the human genome, the mouse genome is being sequenced. Genbank provides about 1.2% of the 3-billion-base mouse genome and a rough draft of the mouse genome is expected to be available by 2003 and a finished genome by 2005. The Drosophila Genome Project has also been completed recently. Thus far, genomes of more than 30 organisms have been sequenced.

Traditional nucleic acid sequencing methods include the chemical cleavage method (or the Maxam-Gilbert method) and the chain termination method (or the Sanger method) (Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual*, 2<sup>nd</sup> Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989). The basic strategy for the chemical cleavage method is to specifically cleave the end-labeled DNA at only one